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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,081	03/11/2004	Laurent Lecanu	1941.012US1	5330

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

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12/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,081	LECANU ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *5 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-18 and 20-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/3/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of March 3, 2008 on September 3, 2008. Claims 1-4, 6-15, 23, 26 are amended. Claims 5, 19 are withdrawn. Claims 29-32 are cancelled.

Claims 1-4, 6-18, 20-28, drawn to a rat with impaired performance in memory and learning and to a method of making said rat, are under consideration.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement (IDS) on September 3, 2008. The IDS has been considered.

Withdrawn Rejections

35 USC § 112, 1st parag., Enablement

Applicant's arguments, see page 6 of Applicant's response, filed September 3, 2008, with respect to the rejection of claims 1-4, 6-18, 20-28 have been fully considered and are persuasive. With regard to the claims being readable on any rodent, Applicant has amended the claims such that the claimed such that the invention is drawn to a rat. The rejection as it applies to this issue is withdrawn. With regard to the use of Abeta protein from any species of animal, Applicant indicates that an abstract by Yamada et al., 1987 teaches that amyloid precursor protein (APP) is highly conserved. In response, this is persuasive and the rejection as it applies to this issue is withdrawn. With regard to the claims reading on the rat having any neurological disease, Applicant

has amended the claims such that the rats exhibit an impaired performance in memory and learning. This is persuasive and the rejection as it applies to this issue is withdrawn. The rejection of claims 1-4, 6-18, 20-28 is withdrawn.

35 USC § 112, 2nd parag.

Applicant's arguments, see page 6 of Applicant's response, filed September 3, 2008, with respect to the rejection of claims 1-4, 6-18, 20-28 have been fully considered and are persuasive. Applicant has amended clam 1 such that the claim is drawn only to a rat. Similarly, claim 15 has been amended such that the claim is drawn only to a rat. The rejection of claims 1-4, 6-18, 20-28 has been withdrawn.

New Rejections

It is noted that Applicant's amendments of claims 1 and 15 have necessitated new grounds of rejection. Instant claim 1's scope has been modified to a rat "with impaired performance in memory and learning." Instant claim 15's scope has been modified to a method of inducing "hyperphosphorylated tau, amyloid plaques, or neurofibrillary tangles."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-14 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Olariu et al., 2001, J. Neural Transm., 108: 1065-1079.

Olariu et al. teach that chronic infusion of beta-amyloid fragment (25-35) at nanomolar concentration into rat cerebral ventricle impairs learning and memory (Olariu et al., abstract). Olariu et al. teach the two major forms of the aggregated beta-amyloid peptide comprising 40 or 42 amino acids have been well described as the prominent components of the senile plaques in AD. Olariu et al. teach that accumulation of amyloid peptides is associated with progressive neuronal death, cognitive deficits, and neuropsychiatric disorder (Olariu et al., page 1065, under Introduction).

It is noted that Olariu et al. meet the limitation of claim 1 with regard to the infused rat exhibiting an impaired learning and memory and that rat exhibits amyloid plaques. As such, Olariu et al. meet the structural limitations of claim 1. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

With regard to Olariu et al. teaching the peptide 25-35 and the claims being drawn to peptide 24-35 (claim 4), as far as can be told, "24-35" and "25-35" are the same fragment.

Thus, Olariu et al. anticipate the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-18, 20-28 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Olariu et al., 2001, J. Neural Transm., 108: 1065-1079 in view of Wertz et al., 1996, TIBS, 21: 359-364, Lin, 2001, Free Radical Biology and Medicine, 30: 225-231.

Olariu et al. teach that chronic infusion of beta-amyloid fragment (25-35) at nanomolar concentration into rat cerebral ventricle impairs learning and memory (Olariu et al., abstract). Olariu et al. teach the two major forms of the aggregated beta-amyloid peptide comprising 40 or 42 amino acids have been well described as the prominent components of the senile plaques in AD. Olariu et al. teach that accumulation of amyloid peptides is associated with progressive neuronal death, cognitive deficits, and neuropsychiatric disorder (Olariu et al., page 1065, under Introduction).

While Olariu et al. teach that infusion of beta-amyloid fragment (25-35) into rat brain result in the rat exhibiting cognitive deficits, Olariu et al. do not teach that the rats were also treated with a pro-oxidative compound, an anti-oxidant inhibitor, a phosphatase inhibitor, and a pro-inflammatory compound.

Wertz et al. teach that a number of molecular reagents were known to induce programmed cell death (PCD). In addition to amyloid (Wertz et al., page 360, 2nd col. under "Tissue amyloid"), these include TNF-alpha (e.g. claims 12-13)(Wertz et al., page 359, 3rd col., under "Receptor ligands") and okadaic acid (e.g. claims 10-11)(Wertz et al., page 362, 1st col. under "Alteration of protein phosphorylation").

With regard to a pro-oxidative compound (e.g. claims 6-7), Lin teaches the neurotoxic effect of zinc and iron. Lin teaches that seven days after intranigral infusion of zinc, lipid peroxidation was elevated in the infused substantia nigra (SN). Pretreatment of rats with butionine sulfoximine (BSO) depleted cellular glutathione (GSH) levels and enhanced zinc-induced oxidative injuries in the nigrostriatal dopaminergic system. Moreover, simultaneous administration of zinc and iron augmented oxidative injuries in the rat brain (Lin, abstract).

All of the component parts are taught by Olariu et al., Wertz et al., and Lin. The only difference is the combination of the "old elements" into a single method of administering beta-amyloid peptide, TNF-alpha, okadaic acid, an iron compound, and BSO. It would have been obvious to one of ordinary skill to combine beta-amyloid peptide, TNF-alpha, okadaic acid, an iron compound, and BSO since Olariu et al., Wertz et al., and Lin teach different ways of inducing cell death in an in vivo system. An artisan would have wanted to induce cell death in the brain because Olariu et al. teach that cell death in the cerebral ventricle results in a model of impaired learning and memory.

With regard to the claims being drawn to metal-sulfate (claims 6, 7) compounds, Lin teaches the use of ferrous ammonium sulfate and zinc chloride (Lin, page 226, 2nd col., under "In vivo study"). However, it was known at the time of filing that ferrous sulfate is a lipid peroxidation product (Pedersen et al., page 405, 2nd col. under "Potencies and effectiveness of Urc, CRH, and UrcII in protecting culture hippocampal neurons from oxidative and excitotoxic insults"). As such, it would have been obvious for an artisan at the time of filing to substitute the ferrous ammonium sulfate taught by Lin with ferrous sulfate because the product of lipid peroxidation, ferrous sulfate enhances oxidative injuries in the cell.

Thus, the claims are obvious.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632